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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,263	02/19/2004	Yoshiyuki Inada	087147-0494	3131

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EXAMINER	
LOEWE, SUN JAE Y	

ART UNIT	PAPER NUMBER
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/781,263	INADA ET AL.	
	Examiner	Art Unit	
	SUN JAE Y. LOEWE	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-30-2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-10 are pending in the instant application.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on October 30, 2007 was filed in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The IDS was considered. A signed copy of form 1449 is enclosed herewith.

Oath/Declaration

3. The reissue oath/declaration filed with this application is defective (see 37 CFR 1.175(a)(1) and MPEP § 1414) because of the following:

a) The foreign priority is not properly claimed (see MPEP 1417); Applicant is requested to utilize the appropriate language for claiming foreign priority:

☐ I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or (f), or 365(b) Attached is form PTO/SB/02B (or equivalent) listing the foreign applications

Forms PTO/SB/51 (inventor oath) and PTO/SB/52 (assignee oath) are suggested for Applicant's use depending on whether the oath is a broadening oath or narrowing oath (respectively). The forms provide guidance for complying with the requirements of 37 CFR 1.175 and 1.63. The forms can be found in MPEP 1414.

b) The acknowledgment for duty to disclose inappropriately identifies 37 CFR 1.56(a). The correct reference is 37 CFR 1.56.

4. The supplemental oath/declaration is defective because it is based on a defective oath/declaration (see above, section 3). Furthermore, the supplemental oath/declaration does not properly identify 37 CFR 1.56.

5. Claims 1-10 rejected as being based upon a defective reissue oath/declaration under 35

U.S.C. 251 as set forth above. See 37 CFR 1.175.

The nature of the defect(s) in the oath/declaration is set forth in the discussion above in this Office action (above, sections 3 and 4).

Specification

6. The specification is objected to because of the following informality. The disclosure (column 10) refers to "verapamyl" and "flunarizim" which appear to be typographical errors of the known calcium antagonists "verapamil" and "flunarizine." Appropriate clarification and/or correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2 and 7-10 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of treating hypertension, does not reasonably provide enablement for the method of treating the broader scope of "angiotensin II-mediated diseases." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916)

which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims
The claims are drawn to method of treating "angiotensin II-mediated diseases." The term "angiotensin II-mediated diseases" broadly encompasses

> "hypertension, cardiac insufficiency, ischemic peripheral circulation disturbances, myocardial ischemia, vein insufficiency, progressive cardiac insufficiency after myocardial infarction, diabetic nephritides, nephritis, arteriosclerosis, hyperaldosteronism, dermatosclerosis, glomerulosclerosis, renal insufficiency, diseases of central nervous system, sensory disturbances including Alzheimer's disease, deficiency of memory, depression, amoesia and senile dementia, anxiety neurosis, catatonia or indisposition, glaucoma, intraocular high tension. ",

(instant specification column 10).

The nature of the invention
Support for the claimed method is based on the in vivo antihypertensive activity, via proposed antagonism of the angiotensin II receptor (instant specification, column 14, 5th paragraph), by the instantly claimed compounds.

The state of the prior art/level of ordinary skill/level of predictability
The antagonism of the angiotensin II receptor is an art recognized methodology for the treatment of hypertension.

An art recognized correlation cannot be drawn between the instant activity and other disorders within the scope of "angiotensin II- mediated disesases" for the representative reasons provided below.

It has been documented that angiotensin II receptor antagonists *may increase the risk of myocardial infarction*. For example, in the VALUE trial (n=15,245), treatment with valsartan (an angiotensin II receptor antagonist) was associated with a statistically

significant increase (19%) in total myocardial infarction. Similarly, losartan and cadesartan clinical trials reported increased myocardial infarction compared with standard (Strauss et al., pg. 843, 2nd column, 3rd paragraph). Myocardial infarction occurs when myocardial ischemia exceeds a critical threshold (Bajzer, C.T.). Thus, the state of the art suggests that angiotensin II receptor antagonism may result in myocardial ischemia.

The art of utilizing angiotensin II receptor antagonism for the treatment of Alzheimer's Disease is nascent. However, evidence suggests a high level of unpredictability in this "nascent" art. See representative facts below:

- Alzheimer's disease is fatal and permanent (see Alzheimer's Disease Treatment Phases)
- There are five medications approved for the treatment of Alzheimer's (Donepezil, galantamine, rivastigmine, tacrine: cholinesterase inhibitors; Memantine: glutamatergic NMDA receptor inhibitor) – (Alzheimer's Drugs, Consumer Reports Best Buy Drugs)
- "Although many have been tried, no other types of medicines have been shown effective in delaying the onset or reducing Alzheimer's symptoms and disabilities (Alzheimer's Drugs, Consumer Reports Best Buy Drugs)

The amount of direction provided by the inventor/existence of working examples
No working examples are provided in the instant specification. The guidance/direction is limited to the in vivo antihypertensive activity of the instantly claimed compounds.

The quantity of experimentation needed to make or use the invention

In the absence of working examples/direction, enablement rests on the existence of an art recognized predictable correlation between the disclosed activity and the claimed use. Evidence suggests that this requirement is not met for the instant case because, for the reasons discussed above, antagonism of the angiotensin II receptor (or antihypertensive activity) does not reasonably correlate with the treatment of the full scope of "angiotensin II mediated diseases."

MPEP 2164.01(a) states:

> There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:
>
> (A) The breadth of the claims;
>
> (B) The nature of the invention;
>
> (C) The state of the prior art;
>
> (D) The level of one of ordinary skill;
>
> (E) The level of predictability in the art;
>
> (F) The amount of direction provided by the inventor;
>
> (G) The existence of working examples; and
>
> (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the evidence regarding each of the above factors (see discussion above), the specification, at the time the application was filed, would not have taught one of ordinary skill in the art how to practice the full scope of the claimed invention without undue experimentation. The experimentation required to practice the claimed invention: a) test the compounds in preclinical trials (which includes initial testing in animal model assays) to determine if the compounds are active for each of the claimed diseases; b) if the compounds are active in animal models advance testing to clinical trials to determine efficacy in treating each of the diseases in humans.

Based on the above analysis, the scope of the instant claims lack enablement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-10 rejected under 35 U.S.C. 103(a) as being obvious over Naka et al. (EP 0520423 and EP 0459136) in view of Weinstock et al. (WO 92/10097), further in view of Wong et al. (caplus AN 91307690). This rejection is directed to the treatment of hypertension, which is enabled.

Determination of the scope and contents of prior art.
Naka et al. teach angiotensin II receptor antagonists (and pharmaceutical compositions thereof) useful for the treatment of hypertension. The following compounds are disclosed:

2-ethoxy-1-{[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl}benzimidazole-7-carboxylic acid (EP 0520423, pg. 31)

2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylic acid (EP 0459136, pg. 21)

1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate (EP 0459136, pg. 22).

Ascertaining the differences between prior art and instant claims.
The instant claims teach:

a) Pharmaceutical compositions comprising one of the above named compounds in combination with a diuretic or calcium antagonist (claims 4-6)
b) Method of treating hypertension using one of the above named compounds in combination with a diuretic or calcium antagonist (claims 7-10)
c) Method of treating hypertension using one of the above named compounds in combination with furosemide (claims 1-3).

The difference between the instant claims and the prior art is the requisite presence of an additional ingredient (ie. diuretic - eg. furosemide or calcium antagonist).

Weinstock et al. teach the combination of angiotensin II antagonists with diuretics (eg. amiloride, metolazone, spironolactone) or calcium antagonists (eg. nicardipine, minodipine, nisoldipine) for the treatment of hypertension (pg. 24-25).

Wong et al. specifically teaches the combination of furosemide (a diuretic) and Dup 753 (an angiotensin II receptor antagonist).

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.
One of ordinary skill would be motivated, from the disclosure in the prior art, to make the modification required to have arrived at the instant invention: ie. combine the claimed compounds with diuretics and/or calcium antagonists for the purpose of treating hypertension.

Furthermore, it is obvious to combine compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose. In re Kerkoven, 205 USPQ 1069 (C.C.P.A. 1980).

Thus, the instant claims are *prima facie* obvious over Naka et al. in view of Weinstock et al. further in view of Wong et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined

application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-10 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8-12, 14-16, 19, 20 and 23-25 of U.S. Patent No. 5,736,555 in view of Weinstock et al. (WO 92/10097), further in view of Wong et al. (caplus AN 91307690).

> *Determination of the scope/contents of claim 1-6, 8-12, 14-16, 19, 20 and 23-25 of US 5,736,555*
> The claims are drawn to a Markush group of compounds, pharmaceutical compositions thereof, and method of use. The utility is the same as that of the instant invention: ie. antagonism of the angiotensin II receptor for the treatment of diseases.

A preferred embodiment is the compound **2-ethoxy-1((2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl)methyl) benzimidazole- 7-carboxylic acid** (see column 144). Although this preferred embodiment is excluded from claims 1-6, 8-12, 14-16, 19, 20 and 23-25, obvious variants of this embodiment are encompassed by the claims: eg. homologs wherein the benzimidazole core is substituted by 2-alkoxy.

A preferred embodiment is the treatment of hypertension (see column 2).

Ascertaining the differences between claims 1-6, 8-12, 14-16, 19, 20 and 23-25 of US 5,736,555 and the claims at issue.
The difference between the preferred embodiments and the instant claims: the instant claims require the presence of an additional ingredient, namely a diuretic or calcium antagonist.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.
MPEP § 2144.08.II.A.4(c) states "…consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties". This is a "Genus-Species Guidelines" for the examination based on 35 U.S.C. 103. An analogous guideline was followed here for the analysis of obviousness-type double patenting.

The preferred embodiments suggests to one of ordinary skill to practice the following invention: make and use **2-ethoxy-1((2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl)methyl) benzimidazole- 7-carboxylic acid** and obvious variants (eg. homologs) for the treatment of hypertension.

The disclosure of Weinstock et al. in view of Wong et al. suggests to one of ordinary skill to modify the above noted preferred embodiment to arrive at the instantly claimed invention: ie. add additional ingredients such as diuretics or calcium antagonists (see Section 8). One of ordinary skill would have reasonable expectation of success in practicing this modified invention. The motivation is to make additional agents, and practice additional methods, for the treatment of hypertension.

Furthermore, it is obvious to combine compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose. In re Kerkoven, 205 USPQ 1069 (C.C.P.A. 1980).

Finally, it is noted that to those skilled in chemical art, one homologue is not an advance over another member of a homologous series. The reason for this is that one of ordinary skill, knowing the properties of one member of series, would know what properties to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963).

Thus, the instant claims are *prima facie* obvious over claims 1-6, 8-12, 14-16, 19, 20 and 23-25 of U.S. Patent No. 5,736,555 in view of Weinstock et al, further in view of Wong et al.

10. Claims 1-10 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8-16, 19, 20 and 23-25 of U.S. Patent No. 5,583,141 in view of Weinstock et al. (WO 92/10097), further in view of Wong et al. (caplus AN 91307690).

Determination of the scope/contents of claims 1-6, 8-16, 19, 20 and 23-25 of US 5,583,141
The claims are drawn to a Markush group of compounds, pharmaceutical compositions thereof, and method of use. The utility is the same as that of the instant invention: ie. antagonism of the angiotensin II receptor for the treatment of diseases.

A preferred embodiment is the compound **2-ethoxy-1((2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl)methyl) benzimidazole- 7-carboxylic acid** (see column 124). Although this preferred embodiment is excluded from claims 1-6, 8-12, 14-16, 19, 20 and 23-25, obvious variants of this embodiment are encompassed by the claims: eg. homologs wherein the benzimidazole core is substituted by 2-alkoxy.

A preferred embodiment is the treatment of hypertension (see column 2).

Ascertaining the differences between claims 1-6, 8-16, 19, 20 and 23-25 of US 5,583,141 and the claims at issue.
The difference between the preferred embodiments and the instant claims: the instant claims require the presence of an additional ingredient, namely a diuretic or calcium antagonist.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.
MPEP § 2144.08.II.A.4(c) states "…consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties". This is a "Genus-Species Guidelines" for the examination based on 35 U.S.C. 103. An analogous guideline was followed here for the analysis of obviousness-type double patenting.

The preferred embodiments suggests to one of ordinary skill to practice the following invention: make and use **2-ethoxy-1((2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl)methyl) benzimidazole- 7-carboxylic acid** and obvious variants (eg. homologs) for the treatment of hypertension.

The disclosure of Weinstock et al. in view of Wong et al. suggests to one of ordinary skill to modify the above noted preferred embodiment to arrive at the instantly claimed invention: ie. add additional ingredients such as diuretics or calcium antagonists (see Section 8). One of ordinary skill would have reasonable expectation of success in practicing this modified invention. The motivation is to make additional agents, and practice additional methods, for the treatment of hypertension.

Furthermore, it is obvious to combine compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose. In re Kerkoven, 205 USPQ 1069 (C.C.P.A. 1980).

Finally, it is noted that to those skilled in chemical art, one homologue is not an advance over another member of a homologous series. The reason for this is that one of ordinary skill, knowing the properties of one member of series, would know what properties to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963).

Thus, the instant claims are *prima facie* obvious over claims 1-6, 8-16, 19, 20 and 23-25 of U.S. Patent No. 5,583,141 in view of Weinstock et al, further in view of Wong et al.

11. Claims 1-10 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,243,054 in view of Weinstock et al. (WO 92/10097), further in view of Wong et al. (caplus AN 91307690).

Determination of the scope/contents of claim 1 of US 5,243,054
The claim is drawn to
2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo- 1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl]ben- zimidazole-7-carboxylic acid. as a therapeutic agent for the treatment of diseases.

A preferred embodiment is the treatment of hypertension (column 2).

Ascertaining the differences between claim 1 of US 5,243,054 and the claims at issue.
The difference between the preferred embodiments and the instant claims: the instant claims require the presence of an additional ingredient, namely a diuretic or calcium antagonist.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.
MPEP § 2144.08.II.A.4(c) states "…consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from

the genus, based on the reasonable expectation that structurally similar species usually have similar properties". This is a "Genus-Species Guidelines" for the examination based on 35 U.S.C. 103. An analogous guideline was followed here for the analysis of obviousness-type double patenting.

The preferred embodiment suggests to one of ordinary skill to practice the following invention: make and use **2-ethoxy-1((2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl)methyl) benzimidazole- 7-carboxylic acid** for the treatment of hypertension.

The disclosure of Weinstock et al. in view of Wong et al. suggests to one of ordinary skill to modify the above noted preferred embodiment to arrive at the instantly claimed invention: ie. add additional ingredients such as diuretics or calcium antagonists (see Section 8). One of ordinary skill would have reasonable expectation of success in practicing this modified invention. The motivation is to make additional agents, and practice additional methods, for the treatment of hypertension.

Furthermore, it is obvious to combine compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose. In re Kerkoven, 205 USPQ 1069 (C.C.P.A. 1980).

Thus, the instant claims are *prima facie* obvious over claim 1 of U.S. Patent No. 5,243,054 in view of Weinstock et al, further in view of Wong et al.

12. Claims 4-10 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,420,405.

The claims are drawn to pharmaceutical compositions comprising, and methods of treating angiotensin II-mediated disease using, the compounds

(±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-3-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylate,

2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or

2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl) biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic

and an additional ingredient which is thrichloromethiazide (a diuretic) or indapamide (a calcium antagonist). The claims anticipate the instant claims.

13. Claims 1-10 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 and 17 of U.S. Patent No. 7,294,344 in view of Weinstock et al. (WO 92/10097), further in view of Wong et al. (caplus AN 91307690).

Determination of the scope/contents of claims 1-15 and 17 of US 7,294,344

The claims are drawn to preparations comprising a compound selected from the group consisting of 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylic acid, 1-(cyclohexyloxycarbonyloxy) ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl] methyl]benzimidazole-7-carboxylate and 2-ethoxy-1-[[2'-(4,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl) biphenyl-4-yl]methyl]benzimidazole-7-carboxylic acid, for the treatment of diseases.

A preferred embodiment is the treatment of hypertension (ie. see claim 17).

Ascertaining the differences between claims 1-15 and 17 of US 7,294,344 and the claims at issue.

The difference between the preferred embodiments and the instant claims: the instant claims require the presence of an additional ingredient, namely a diuretic or calcium antagonist.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

MPEP § 2144.08.II.A.4(c) states "…consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties". This is a "Genus-Species Guidelines" for the examination based on 35 U.S.C. 103. An analogous guideline was followed here for the analysis of obviousness-type double patenting.

The preferred embodiment suggests to one of ordinary skill to practice the following invention: make and use the above noted compounds for the treatment of hypertension.

The disclosure of Weinstock et al. in view of Wong et al. suggests to one of ordinary skill to modify the above noted preferred embodiment to arrive at the instantly claimed invention: ie. add additional ingredients such as diuretics or calcium antagonists (see Section 8). One of ordinary skill would have reasonable expectation of success in practicing this modified invention. The motivation is to make additional agents, and practice additional methods, for the treatment of hypertension.

Furthermore, it is obvious to combine compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose. In re Kerkoven, 205 USPQ 1069 (C.C.P.A. 1980).

For the reasons discussed above, the instant claims are *prima facie* obvious over claim 1-15 and 17 of U.S. Patent No. 7,294,344 in view of Weinstock et al, further in view of Wong et al.

14. Claims 1-10 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4-14, 19 and 25-27 of U.S. Patent No. 6,589,547 in view of Weinstock et al. (WO 92/10097), further in view of Wong et al. (caplus AN 91307690).

Determination of the scope/contents of claims 1, 2, 4-14, 19 and 25-27 of US 6,589,547
The claims are drawn to preparations comprising a compound having angiotensin II antagonistic activity for the treatment of diseases.

A preferred embodiment is the treatment of hypertension (claim 19).

Preferred embodiments are preparations comprising the compounds of:

2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl] benzimidazole-7-carboxylic acid; 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-benzimidazole-7-carboxylate; or 2-ethoxy-1-[[2'-(4,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylic acid.

Ascertaining the differences between claims 1, 2, 4-14, 19 and 25-27 of US 6,589,547 and the claims at issue.
The difference between the preferred embodiments and the instant claims: the instant claims require the presence of an additional ingredient, namely a diuretic or calcium antagonist.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.
MPEP § 2144.08.II.A.4(c) states "…consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties". This is a "Genus-Species Guidelines" for the examination based on 35 U.S.C. 103. An analogous guideline was followed here for the analysis of obviousness-type double patenting.

The preferred embodiment suggests to one of ordinary skill to practice the following invention: make and use the above noted compounds for the treatment of hypertension.

The disclosure of Weinstock et al. in view of Wong et al. suggests to one of ordinary skill to modify the above noted preferred embodiment to arrive at the instantly claimed invention: ie. add additional ingredients such as diuretics or calcium antagonists (see Section 8). One of ordinary skill would have reasonable expectation of success in practicing this modified invention. The motivation is to make additional agents, and practice additional methods, for the treatment of hypertension.

Furthermore, it is obvious to combine compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose. In re Kerkoven, 205 USPQ 1069 (C.C.P.A. 1980).

For the reasons discussed above, the instant claims are *prima facie* obvious over claim 1, 2, 4-14, 19 and 25-27 of U.S. Patent No. 6,589,547 in view of Weinstock et al, further in view of Wong et al.

Conclusion

15. No claims allowed.

16. Applicant is reminded of the continuing obligation under 37 CFR 1.178(b), to timely apprise the Office of any prior or concurrent proceeding in which Patent No. 6,348,482 is or was involved. These proceedings would include interferences, reissues, reexaminations, and litigation.

Applicant is further reminded of the continuing obligation under 37 CFR 1.56, to timely apprise the Office of any information which is material to patentability of the claims under consideration in this reissue application.

These obligations rest with each individual associated with the filing and prosecution of this application for reissue. See also MPEP §§ 1404, 1442.01 and 1442.04.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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